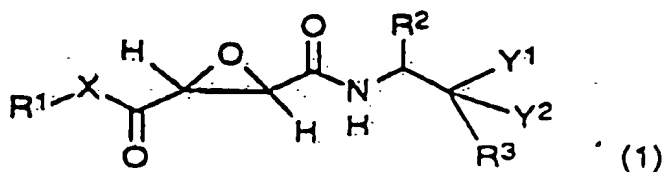


28. (Twice Amended) An epoxysuccinamide derivative having the following formula (1) and its physiologically acceptable salt:



wherein

R<sup>1</sup> represents a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10 carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, or an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

R<sup>2</sup> represents an isobutyl group or an isopropyl group;

R<sup>3</sup> represents a hydrogen atom or an aryl group having 6 to 20 carbon atoms;

X represents -O- or -NR<sup>4</sup>- in which R<sup>4</sup> is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

Y<sup>1</sup> represents OR<sup>5</sup> is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, an acyl group having 2 to 20 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms; and

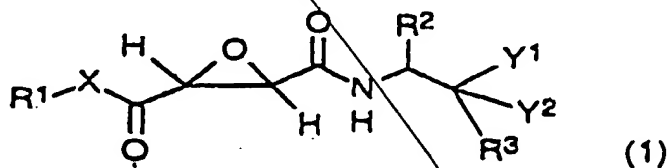
Y<sup>2</sup> represents a hydrogen atom;

Sub  
D2  
provided that the alkyl group for R<sup>5</sup> may have one or more substituents selected from the group consisting of hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, and guanidino;

provided that the aryl group for R<sup>1</sup>, R<sup>3</sup> and R<sup>5</sup> may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino; and

provided that the heterocyclic group for R<sup>5</sup> may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino.

34. (Twice Amended) A method for treating bone diseases which comprises injecting or orally administering into a patient an epoxysuccinamide derivative having the following formula (1) and its physiologically acceptable salt in an amount of 0.01 to 100 mg/day in the case of injection or in an amount of 0.1 mg/day to 1 g/day in the case of oral administration:



Sub  
03  
02  
wherein

$R^1$  represents a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10 carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, or an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

$R^2$  represents an isobutyl group or an isopropyl group;

$R^3$  represents a hydrogen atom or an aryl group having 6 to 20 carbon atoms;

X represents -O- or -NR<sup>4</sup>- in which  $R^4$  is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

$Y^1$  represents OR<sup>5</sup> is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, an acyl group having 2 to 20 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms; and

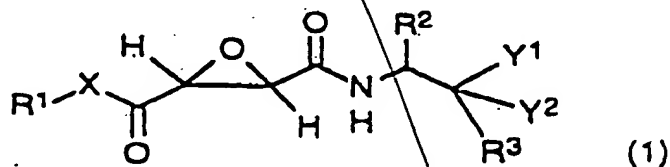
$Y^2$  represents a hydrogen atom;

provided that the alkyl group for  $R^5$  may have one or more substituents selected from the group consisting of hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, and guanidino;

506  
D3  
provided that the aryl group for R<sup>1</sup>, R<sup>3</sup> and R<sup>5</sup> may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino; and

provided that the heterocyclic group for R<sup>5</sup> may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino.

35. (Twice Amended) A method for treating arthritis which comprises injecting or orally administering into a patient an epoxysuccinamide derivative having the following formula (1) and its physiologically acceptable salt in an amount of 0.01 to 100 mg/day in the case of injection or in an amount of 0.1 mg/day to 1 g/day in the case of oral administration:



wherein

*2*  
 $R^1$  represents a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10 carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, or an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

*5, 6, 03*  
 $R^2$  represents an isobutyl group or an isopropyl group;

$R^3$  represents a hydrogen atom or an aryl group having 6 to 20 carbon atoms;

$X$  represents  $-O-$  or  $-NR^4-$  in which  $R^4$  is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

$Y^1$  represents  $OR^5$  is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, an acyl group having 2 to 20 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms; and

$Y^2$  represents a hydrogen atom;

provided that the alkyl group for  $R^5$  may have one or more substituents selected from the group consisting of hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, and guanidino;

Sub  
D3

provided that the aryl group for  $R^1$ ,  $R^3$  and  $R^5$  may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino; and

provided that the heterocyclic group for  $R^5$  may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino.

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